

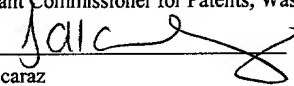
H 2

**CERTIFICATE OF MAILING BY "EXPRESS MAIL"**

Express Mail Label No.: EV093212901US

Date of Deposit: March 15, 2002

I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10 on the date indicated above and is addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

  
Tamara Alcaraz

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In the application of:

Jianming XIAO et al.

Serial No.: 10/080,274

Filing Date: February 19, 2002

For: METHOD AND APPARATUS BASED  
ON BUNDLED CAPILLARIES FOR  
HIGH THROUGHPUT SCREENING

Examiner: To Be Assigned

Group Art Unit: To Be Assigned

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

Prior to examination please enter the following preliminary amendments. A clean copy for publication of the application is enclosed herewith. Please amend the above-identified application as follows:

20051204 14:30:00

## AMENDMENTS

### In the Specification:

Please replace paragraph [0002] with the following:

[0002] This application is a continuation-in-part of U.S. Application Ser. No. 09/791,410 entitled "Method and Apparatus Based on Bundled Capillaries For High Throughput Screening" by Jianming Xiao et al., filed February 22, 2001 and claims the benefit of priority to the following U.S. Applications: U.S. Application Ser. No. 60/269,642, entitled "Method And Apparatus Based On Bundled Capillaries For High Throughput Screening" by Jianming Xiao et al., filed Feb. 16, 2001; U.S. Application Ser. No. 60/271,002, entitled "Liquid Arrays" by Shiping Chen et al., filed Feb. 22, 2001; U.S. Ser. No. 60/302,735, entitled "Picoliter Fluid Delivery" filed Jul. 3, 2001; U.S. App. Ser. No. 60/314,747, entitled "Desktop Drug Screening System," filed Aug. 24, 2001; U.S. App. Ser. No. 60/315,285, entitled "Desktop Drug Screening System," filed Aug. 27, 2001; U.S. Ser. No. 60/327,686, entitled "Single Use XHTS Chip", filed Oct. 4, 2001; U.S. App. Ser. No. not yet assigned, entitled "Reagent Metering", by Shiping Chen, filed Feb. 15, 2002, and U.S. Application Ser. No. 09/791,411, entitled "Liquid Arrays" by Shiping Chen et al., filed February 22, 2001. All of the above applications are incorporated by reference herein in their entireties as if fully set forth below for all purposes.

Two page 21's were submitted with the application. Please delete the version of "page 21" a red-lined copy of which is submitted herewith.

Please replace paragraph [0093] with the following:

[0093] In a third configuration, referred to as a "chip" format, as shown in Figure 7C, all through holes are formed in a solid piece, which takes a chip shape having a top 680 and a bottom 690 surface where probe liquids may enter and exit the through holes. Similar to the previously described formats, the diameters of the holes are sufficiently small and inner surfaces of the holes are sufficiently hydrophilic such that liquid probes are retained within the channel by

capillary force. The thickness of the chip 692, and hence the length of the through holes, can range from about 50 $\mu$ m to several tens of centimeters preferably ranging from 200 $\mu$ m to 1 centimeter, more preferably 500  $\mu$ m to 2 millimeters. The size of a chip can be as small as 1mmX1mm, as large as 130mmX130mm. The through hole pattern can be randomly or orderly distributed. In the case of orderly distributed hole pattern, the hole pattern matches that of the delivery head capillary, or, in another example, matches the well pattern of a microtiter plate (96, 384, 1536, 3072, or 6144 well). A chip with microtiter plate pattern can be used as a "compound library cover" for a microtiter plate. The size of the chip can range from 5,000 cm<sup>2</sup> to 0.01 cm<sup>2</sup>, or preferably from 1,000cm<sup>2</sup> to 0.1cm<sup>2</sup>, or more preferably from 100cm<sup>2</sup> to 1 cm<sup>2</sup>. The array of assaying sites on the assaying surface has a spatial pitch ranging from 10mm to 1 $\mu$ m, or preferably 1mm to 10 $\mu$ m, more preferably 500  $\mu$ m to 50  $\mu$ m. The cross-section of the through hole may be circular or any other shape. Further, it may have the same shape and dimension along its length, or more preferably, it is structured to provide additional assaying functions as described in detail later. The through hole structure may have branches or junctions that involve multiple paths. In most cases, the through hole has its second opening on a second surface that is substantially parallel to the first surface, where the first opening of the through hole exits. It is also possible that the second opening of the through hole exits on the same surface as the first one. The diameter of the through hole ranges from 10mm to 0.1 $\mu$ m, or preferably from 1 mm to 1 $\mu$ m, more preferably from 400 $\mu$ m to 10 $\mu$ m.

**REMARKS**

The specification has been amended to correct the priority information and to delete one of two copies of page 21 submitted with the original application. The material added to paragraph 93 was originally submitted in the version of the "page 21" now deleted. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made**".

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 473532000620. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: March 15, 2002

By:



Shantanu Basu  
Registration No. 43,318

Morrison & Foerster LLP  
755 Page Mill Road  
Palo Alto, California 94304-1018  
Telephone: (650) 813-5995  
Facsimile: (650) 494-0792

VERSION WITH MARKINGS TO SHOW CHANGES MADE

**In the Specification:**

Please replace paragraph [0002] with the following:

[0002] This [invention] application is a continuation-in-part of U.S. Application Ser. No. 09/791,410 entitled "Method and Apparatus Based on Bundled Capillaries For High Throughput Screening" by Jianming Xiao et al., filed February 22, 2001 and claims the benefit of priority to the following U.S. Applications: U.S. Application Ser. No. 60/269,642, entitled "Method And Apparatus Based On Bundled Capillaries For High Throughput Screening" by Jianming Xiao et al., filed Feb. 16, 2001; U.S. Application Ser. No. 60/271,002, entitled "Liquid Arrays" by Shiping Chen et al., filed Feb. 22, 2001; U.S. Ser. No. 60/302,735, entitled "Picoliter Fluid Delivery" filed Jul. 3, 2001; U.S. App. Ser. No. 60/314,747, entitled "Desktop Drug Screening System," filed Aug. 24, 2001; U.S. App. Ser. No. 60/315,285, entitled "Desktop Drug Screening System," filed Aug. 27, 2001; U.S. Ser. No. 60/327,686, entitled "Single Use XHTS Chip", filed Oct. 4, 2001; [and] U.S. App. Ser. No. not yet assigned, entitled "Reagent Metering", by Shiping Chen, filed Feb. 15, 2002, and U.S. Application Ser. No. 09/791,411, entitled "Liquid Arrays" by Shiping Chen et al., filed February 22, 2001. All of the above applications are incorporated by reference herein in their entireties as if fully set forth below for all purposes.

Two page 21's were originally submitted. Please delete the entire page 21 which reads as follows (A red-lined copy of the "page 21" to be deleted is also submitted):

[example, a bundle of 1m in length with a cavity diameter of 20µm can store 0.3µl probe liquid, sufficient for hundreds of experiments.

**II.A.3 Chip Format**

[0048 [0052] \_\_\_\_\_ In a third configuration, referred to as a "chip" format, as shown in Figure 7C, all through holes are formed in a solid piece, which takes a chip shape having an top 680 and a bottom 690 surface where probe liquids may enter and exit the through holes. Similar to the

previously described formats, the diameters of the holes are sufficiently small and inner surfaces of the holes are sufficiently hydrophilic such that liquid probes are retained within the channel by capillary force. The thickness of the chip 692, and hence the length of the through holes, can range from about 50 $\mu$ m to several tens of centimeters. The size of a chip can be as small as 1mmX1mm, as large as 130mmX130mm. The through hole pattern can be randomly or orderly distributed. In the case of orderly distributed hole pattern, the hole pattern matches that of the delivery head capillary, or, in another example, matches the well pattern of a microtiter plate (96, 384, 1536, 3072, or 6144 well). A chip with microtiter plate pattern can be used as a "compound library cover" for a microtiter plate.

[0049] [0053] The capillary array chip can be fabricated in many different ways. It may be assembled from bundling ready-made individual long capillary tubes through out the entire length. The bundling ready-made individual long capillary tubes through out the entire length. The bundling can be achieved through epoxy or fusion bonding. The long bundle is then cut to desired length. The second way is to bundle large preform tubes together and extrude the preform bundle into a long solid capillary bundle, then cut into desired length. The third way is to mold a large preform of through hole array with a suitable powder mixture, usually made of ceramics or metal oxide. The mold is solidified]

Please replace paragraph [0093] with the following:

[0093] In a third configuration, referred to as a "chip" format, as shown in Figure 7C, all through holes are formed in a solid piece, which takes a chip shape having a top 680 and a bottom 690 surface where probe liquids may enter and exit the through holes. Similar to the previously described formats, the diameters of the holes are sufficiently small and inner surfaces of the holes are sufficiently hydrophilic such that liquid probes are retained within the channel by capillary force. The thickness of the chip 692, and hence the length of the through holes, can range from about 50µm to several tens of centimeters preferably ranging from 200µm to 1 centimeter, more preferably 500 µm to 2 millimeters. The size of a chip can be as small as 1mmX1mm, as large as 130mmX130mm. The through hole pattern can be randomly or orderly distributed. In the case of orderly distributed hole pattern, the hole pattern matches that of the delivery head capillary, or, in another example, matches the well pattern of a microtiter plate (96, 384, 1536, 3072, or 6144 well). A chip with microtiter plate pattern can be used as a "compound library cover" for a microtiter plate. The size of the chip can range from 5,000 cm<sup>2</sup> to 0.01 cm<sup>2</sup>, or preferably from 1,000cm<sup>2</sup> to 0.1cm<sup>2</sup>, or more preferably from 100cm<sup>2</sup> to 1 cm<sup>2</sup>. The array of assaying sites on the assaying surface has a spatial pitch ranging from 10mm to 1µm, or preferably 1mm to 10µm, more preferably 500 µm to 50 µm. The cross-section of the through hole may be circular or any other shape. Further, it may have the same shape and dimension along its length, or more preferably, it is structured to provide additional assaying functions as described in detail later. The through hole structure may have branches or junctions that involve multiple paths. In most cases, the through hole has its second opening on a second surface that is substantially parallel to the first surface, where the first opening of the through hole exits. It is also possible that the second opening of the through hole exits on the same surface as the first one. The diameter of the through hole ranges from 10mm to 0.1µm, or preferably from 1 mm to 1µm, more preferably from 400µm to 10µm.

example, a bundle of 1m in length with a cavity diameter of 20 $\mu$ m can store 0.3 $\mu$ l probe liquid, sufficient for hundreds of experiments.

### II.A.3 Chip Format

{0048}—{0052} In a third configuration, referred to as a “chip” format, as shown in Figure 7C, all through holes are formed in a solid piece, which takes a chip shape having an top 680 and a bottom 690 surface where probe liquids may enter and exit the through holes. Similar to the previously described formats, the diameters of the holes are sufficiently small and inner surfaces of the holes are sufficiently hydrophilic such that liquid probes are retained within the channel by capillary force. The thickness of the chip 692, and hence the length of the through holes, can range from about 50 $\mu$ m to several tens of centimeters. The size of a chip can be as small as 1mmX1mm, as large as 130mmX130mm. The through hole pattern can be randomly or orderly distributed. In the case of orderly distributed hole pattern, the hole pattern matches that of the delivery head capillary, or, in another example, matches the well pattern of a microtiter plate (96, 384, 1536, 3072, or 6144 well). A chip with microtiter plate pattern can be used as a “compound library cover” for a microtiter plate.

{0049}—{0053} The capillary array chip can be fabricated in many different ways. It may be assembled from bundling ready-made individual long capillary tubes through out the entire length. The bundling can be achieved through epoxy or fusion bonding. The long bundle is then cut to desired length. The second way is to bundle large preform tubes together and extrude the preform bundle into a long solid capillary bundle, then cut into desired length. The third way is to mold a large preform of through hole array with a suitable powder mixture, usually made of ceramics or metal oxide. The mold is solidified